

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

National Institute of Dental and Craniofacial Research

National Advisory Dental and Craniofacial Research Council

Summary Minutes

Date: June 10, 2002

Place: Building 45, Conference Room E-1 & 2
National Institutes of Health
Bethesda, Maryland 20892

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

MINUTES OF THE
NATIONAL ADVISORY DENTAL AND CRANIOFACIAL RESEARCH COUNCIL

June 10, 2002

The 168th meeting of the National Advisory Dental and Craniofacial Research Council (NADCRC) was convened on June 10, 2002, at 8:30 a.m., in Building 45, Conference Room E-1 & 2, National Institutes of Health (NIH), Bethesda, Maryland. The meeting was open to the public from 8:30 a.m. to 12:15 p.m., followed by the closed session for Council business and consideration of grant applications from 1:30 p.m. until adjournment at 4:00 p.m. Dr. Lawrence A. Tabak presided as Chair.

Members Present:

Dr. John Alderete
Dr. Louise Chow
Dr. Nereyda Clark
Dr. Samuel F. Dworkin
Dr. Raymond Fonseca
Dr. Jay Alan Gershen
Dr. Howard Kuramitsu
Dr. Frank Macrina
Dr. Harold Morris
Dr. Linda C. Niessen
Dr. Dianne E. Rekow
Dr. Martha J. Somerman
Ms. Kim S. Uhrich

Members of the Public Present:

Dr. Steve Rawls, Executive Director, American College of Dentists, Rockville, MD
Mr. Jack Bresch, Associate Executive Director, American Dental Education Association (ADEA), Washington, DC
Dr. Aida Chohayeb, Professor, Howard University, Washington, DC
Dr. John Clarkson, President, International Association for Dental Research (IADR), Alexandria, VA
Dr. Robert J. Collins, Deputy Executive Director, American Association for Dental Research (AADR), Alexandria, VA
Ms. Julie Connoyer, Public Policy and Advocacy Program Assistant, ADEA, Washington, DC

Dr. Graham Emery, Past President, IADR, Alexandria, VA
Dr. Karl Haden, Associate Executive Director for Educational Policy and Research, ADEA, Washington, DC
Ms. Gina Luke, Director, State Government Relations and Advocacy Outreach, ADEA, Washington, DC
Ms. Myla Moss, Director, Congressional Relations, ADEA, Washington, DC
Mr. Jonathan Schuermann, Ph.D. Candidate, University of Missouri, Columbia, MO
Dr. Eli Schwarz, Executive Director, AADR and IADR, Alexandria, VA
Dr. John Sauk, Chair, Oral and Maxillofacial Pathology, Department of Pathology, University of Maryland, Baltimore, MD

Federal Employees Present:

National Institute of Dental and Craniofacial Research:

Dr. Lawrence A. Tabak, Director, NIDCR
Dr. Dushanka V. Kleinman, Deputy Director, NIDCR, and Director, Division of Population and Health Promotion Sciences (DPHPS)
Dr. Margo Adesanya, Senior Scientist and Program Director, Patient-Oriented Research Program, DPHPS
Ms. Carolyn Baum, Committee Management Specialist and Council Secretary, Office of the Director (OD)
Ms. Inni Belfer, Fellow, Pain Branch, Division of Intramural Research (DIR)
Dr. Henning Birkedal-Hansen, Scientific Director, NIDCR, and Director, DIR
Dr. Norman S. Braveman, Assistant to the Director, OD
Dr. Patricia S. Bryant, Health Scientist Administrator and Program Director, Behavioral and Social Science Research Program, DPHPS
Dr. Maria Teresa Canto, Health Scientist Administrator and Program Director, Population Studies Program, DPHPS
Dr. Lois K. Cohen, Associate Director of International Health, NIDCR, and Director, Office of International Health (OIH)
Mr. George J. Coy, Chief, Office of Administrative Management (OAM)
Ms. Trenita Davis, Statistical Assistant, DPHPS
Ms. Jody Dove, Public Information Specialist, Public Information and Liaison Branch (PILB), Office of Communications and Health Education (OCHE)
Mr. William Foley, Grants Management Specialist, Division of Extramural Activities (DEA)
Dr. Philip Fox, Consultant, DPHPS
Dr. Isabel Garcia, Special Assistant for Science Transfer, OCHE, and Co-Director, NIDCR Dental Public Health Residency Program
Ms. Christen Gibbons, Computer Specialist, Office of Information Technology (OIT)
Dr. Sarah Glavin, Evaluation Officer, Office of Science Policy (OSPA), OD
Dr. Kevin Hardwick, International Health Officer, OIH
Dr. George Hausch, Acting Director, DEA
Ms. Lorraine Jackson, Extramural Research Coordinator and Outreach Specialist, DPHPS
Ms. Susan M. Johnson, Chief, PILB, OCHE
Mr. William M. Johnston, Consultant, Division of Basic and Translational Sciences (DBTS)

Ms. Mary Kelly, Program Assistant, PILB, OCHE
Dr. Eleni Kousvelari, Chief, Cellular and Molecular Biology, Physiology, and Biotechnology Branch, DBTS
Ms. Wendy A. Liffers, Director, OSPA, OD
Dr. James A. Lipton, Acting Deputy Director, DPHPS, and Director, Research Training and Career Development Program, DPHPS
Dr. Yujing Liu, Scientific Review Administrator, DEA
Dr. Dennis F. Mangan, Chief, Cellular and Molecular Biology Branch, DBTS
Dr. J. Ricardo Martinez, Executive Secretary, NADCRC, and Associate Director for Program Development, OD
Dr. Ruth Nowjack-Raymer, Health Scientist Administrator and Program Director, Health Disparities Research Program, DPHPS
Dr. Ann L. Sandberg, Acting Director, DBTS
Dr. Anna Sandberg, Scientific Review Administrator, Division of Research Activities (DRA)
Dr. Robert Selwitz, Senior Epidemiologist and Co-Director, NIDCR Dental Public Health Residency Program, DPHPS
Dr. Yasaman Shirazi, Health Scientist Administrator, DBTS
Dr. Rochelle Small, Health Scientist Administrator, DBTS
Mr. Robert Tarwater, Grants Management Specialist, DRA
Ms. Tracy Walker, Committee Management Assistant, OD
Ms. Anne Welkener, Grants Management Specialist, DRA
Ms. Dolores A. Wells, Program Analyst, OD
Ms. Mary Ann Williamson, Computer Specialist, OIT
Dr. Guo H. Zhang, Health Scientist Administrator, DBTS

Other Federal Employees:

Dr. C. R. Buchanan, Acting Assistant Medical Director for Dentistry, Department of Veterans Affairs, Washington, DC
Dr. Susan Goodman, Dental Officer, Bureau of Health Professions, Health Resources and Services Administration, Rockville, MD
Dr. Robert Mecklenburg, Consultant, National Cancer Institute, NIH
Ms. Patti Mitchell, Program Analyst, Foreign Agricultural Service, U.S. Department of Agriculture, Alexandria, VA

OPEN PORTION OF THE MEETING

I. CALL TO ORDER

Dr. Lawrence A. Tabak, Director, NIDCR, called the meeting to order. He welcomed and introduced three new members to the Council: Drs. Louise Chow, Nereyda Clark, and Frank Macrina. Dr. Tabak noted that Dr. Jay Gershen has agreed to extend his term on the Council. He invited all attendees to introduce themselves.

Dr. Tabak noted that the agenda for the meeting includes the culmination of substantial work by NIDCR staff over the past 22 months to lay the groundwork for enhancing the Institute's portfolio in translational research. The cornerstone of this portfolio is seven initiatives which staff have developed and which they presented later during the meeting (see section VI below). The initiatives pertain to translational and clinical research on dental caries, tobacco use, temporomandibular disorders, restoration of orofacial tissues, and HIV/AIDS. In several information items, also presented, NIDCR describes its future approach to clinical trials research and an effort to enhance oral health research in the curriculum of dental schools (see section VII).

Dr. Tabak said that NIDCR received important feedback from the public on the Institute's scientific initiatives for Fiscal Year (FY) 2004 and beyond. The period for public comment is now closed. The research themes of these initiatives include molecular anatomy (in pain, head and neck cancer, periodontal diseases), clinical genetics of oral and craniofacial diseases, Sjögren's disease, and HIV/AIDS. Dr. Tabak noted that NIDCR would lengthen the periods of public comment in the future and maintain a transparent planning process.

II. APPROVAL OF MINUTES

The minutes of the Council's meeting on January 28, 2002, were considered and unanimously approved.

III. FUTURE COUNCIL MEETING DATES

The following dates for future Council meetings were confirmed:

September 26-27, 2002

February 3-4, 2003

June 16-17, 2003

September 18-19, 2003

January 20-21, 2004

May 24-25, 2004

September 27-28, 2004

On August 22, 2002, the Council will hold a telephone conference to give second-level review of applications submitted in response to Requests for Applications (RFAs) for funding in FY 2002.

IV. REPORT OF THE DIRECTOR

Dr. Tabak highlighted several items from the written Director's Report (see Attachment III). He reported that he continues to obtain invaluable feedback by meeting with students and faculty at U.S. dental schools and with leaders of professional organizations. He thanked Dr. Gershen for inviting him to visit the newly redesigned and integrated health sciences center at the University of Colorado.

NIH Budget and Personnel. Dr. Tabak referred the Council to the written Director's Report for an update on the FY 2002 budget, the details of the President's Budget for FY 2003, and a summary of the March and April congressional hearings on the President's Budget. He reported that Dr. Elias Zerhouni became the new Director, NIH, effective May 20, and that Dr. Roderic Pettigrew has been named the first permanent director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB).

Scientific Advances. Dr. Tabak also referred the Council to the many scientific advances described in the written Director's Report. He highlighted the discovery of a first gene involved in gingival overgrowth. NIDCR-supported researchers at the University of Pittsburgh, Pennsylvania, identified the SOS1 gene, which when mutated, activates the *ras* pathway and triggers hereditary gingival fibromatosis. Dr. Tabak noted that the discovery could lead to a molecular approach for the repair of gingival tissues and underscores the intrinsic value of studying the so-called rare diseases.

Meetings and Workshops. NIDCR hosted the third annual Patient Advocates Forum on May 2. The forum was attended by 15 advocates for patients who represented 12 organizations that share interest in the oral health effects of their respective disorders and conditions. The participants heard in-depth information on clinical trials and viewed an interactive presentation of the clinicaltrials.gov Web site presented by staff of the National Library of Medicine.

The first annual meeting of the Centers for Research to Reduce Oral Health Disparities (CRROHDs) was held at the NIH on February 25-26. The discussions at the meeting focused on the centers as a national resource, training and career development plans, and evaluation components and strategies.

NIDCR Personnel. Dr. Bruce L. Pihlstrom will join NIDCR on July 1 as Acting Director, Division of Population and Health Promotion Sciences (DPHPS). Presently holding the Erwin Schaffer Chair for Periodontal Research at the University of Minnesota School of Dentistry, Dr. Pihlstrom is a periodontist with extensive experience in clinical research and, in particular, clinical trials. Dr. Tabak noted that Dr. Dushanka V. Kleinman, Deputy Director, NIDCR, has been serving as Director, DPHPS, since its inception, and is also Chief Dental Officer of the Public Health Service Commissioned Corps. He and the Council formally thanked Dr. Kleinman, with applause, for her efforts in "wearing three hats" during the past year.

Additional information on these and other NIDCR activities is provided in the written Director's Report (Attachment III).

V. UPDATES

NIDCR staff members presented updates on four activities previously presented to the Council.

Evaluation

Dr. Sarah Glavin, Evaluation Officer, NIDCR, summarized progress on four major ongoing evaluation projects and elaborated on the key components and current status of one of these projects, a comprehensive review of NIDCR's portfolio of research on caries and periodontal disease. She noted that staff continue to develop an overall evaluation plan in conjunction with the Institute's strategic planning process. The evaluation plan will be a component of the strategic plan (see "Update of NIDCR Strategic Plan" below). In addition, staff have initiated a review of publications of NIDCR-supported investigators in the Centers for Discovery that NIDCR funded several years ago. To prepare for the competing renewal of the P60 center grants, the Institute is piloting the review as a potential approach for reviewing all NIDCR-supported large-scale grants. NIDCR also is initiating a review of its entire portfolio of research on health disparities, including the CRROHDs. For this review, staff are using a unique prospective approach to collect data for future evaluation.

The review of NIDCR research on caries and periodontal disease is the first in a series of planned comprehensive evaluations of segments of the Institute's portfolio. Staff expect to complete collection and preliminary analyses of the data this summer and to convene three expert panels during the fall. The panels, which will include experts in caries, periodontal diseases, and oral-health-related fields, will focus separately on caries, periodontal diseases, and cross-cutting areas and will help NIDCR analyze preliminary findings and develop conclusions. NIDCR expects to complete this review in early 2003 and to present the findings to the Council in January 2003.

Dr. Glavin invited the Council to provide input on the review process and evaluation measures. The review will include all NIDCR-supported grants and intramural projects in caries and periodontal diseases from FY 1996 through FY 2000. The key components of the review include a detailed descriptive analysis of grants and intramural projects and other related activities; bibliometric and content analysis of the literature to compare publications supported by NIDCR with all literature on caries and periodontal diseases and with that supported by other funding sources; analysis of investigators supported by NIDCR (e.g., distribution of grants and publications by investigator, characteristics of the most prolific investigators, investigators' other funding sources); analysis of institutions receiving support from NIDCR (e.g., distribution of grants by institution, characteristics of institutions); assessment of NIDCR-supported training (e.g., distribution of awards, subsequent accomplishments of trainees); and determination of the impact of NIDCR funding (e.g., interventions resulting from research, economic and social impact).

Discussion. The Council applauded NIDCR for implementing a systematic evaluation process. Members asked about the apparent use of only quantitative measures, the need to demonstrate research results in relation to the recent doubling of the NIH budget, the importance of data from industry, and the tracking of research trainees. Dr. Glavin described how more qualitative considerations (e.g., the nature of publications and journals of publication, research progress over time) are also being included. She also noted that NIDCR would be incorporating an evaluation component to identify annually the grants that NIDCR would not have been able to support without

additional funding. She commented on the difficulty of accessing follow-up data on trainees. NIDCR will be field-testing approaches to the construction of a database of all NIDCR-supported extramural and intramural trainees.

Long-Range Scientific Opportunities and Research Agenda

Dr. J. Ricardo Martinez, Associate Director for Program Development, Office of the Director, NIDCR, reported on recent activities of the Scientific Opportunities Work Group. Dr. Tabak charged this group, which consists of staff representing each NIDCR division, to identify and catalog scientific opportunities for 2004-09. As reported at the Council's previous meeting in January, the work group identified three broad research themes: (a) genomics/proteomics of oral, dental, and craniofacial diseases; (b) repair and regeneration of oral, dental, and craniofacial tissues; and (c) clinical and community-based approaches to the diagnosis, prevention, and treatment of oral, dental, and craniofacial disorders. The group recommended that NIDCR convene small expert panels in each area to identify specific areas of scientific opportunity, catalog the resources required to address these opportunities successfully, and suggest ways for NIDCR to make the research community aware of these opportunities.

Dr. Martinez reported that the first panel, on genomics/proteomics, met on May 22 and the report is being finalized at this time. The panel's report will be sent to all Council members and will be disseminated on the NIDCR Web site (www.nidcr.nih.gov). Staff are planning to convene the panel on repair and regeneration in late June-early July and the panel on clinical and community-based approaches by the end of the summer.

The office of Dr. Martinez has also organized other panels. A panel on training met on June 7 to address specific issues in ongoing training programs (e.g., the T32 and T35 programs), possible new programs (e.g., a mentor award), and approaches to training in emerging areas such as genomics. Council member Dr. John Alderete participated on this panel. The report is also being prepared at this time and will be distributed to Council. Another panel focusing on AIDS will be convened in the fall to follow up on a previous NIDCR panel on AIDS which met on April 16 to identify opportunities for FY 2004. Dr. Alderete was a member of the previous AIDS panel.

Discussion. Dr. Martinez noted that NIDCR will ask the panel on clinical and community-based approaches to carefully define the term "community-based" and to include population-based and epidemiological studies in its discussions. Dr. Alderete urged NIDCR to invite directors of community-based organizations to participate on this panel.

Update of NIDCR Strategic Plan

Dr. Tabak reported that NIDCR is initiating an update of its strategic plan. Dr. Isabel Garcia, Special Assistant for Science Transfer, Office of Communications and Health Education, will lead this effort. Dr. Garcia described the Institute's plans and progress to date. She noted that many events have occurred since NIDCR released its first strategic plan in June 1997. The Institute has celebrated its 50th anniversary, changed its name, gained a new director, continued

to mature and grow, led the Surgeon General's review of oral health in America, and made many scientific discoveries.

For the current effort, NIDCR will assess the status of the existing plan and prepare a scientific update that captures blossoming areas of research. Dr. Garcia noted that NIDCR intends to develop a document that is as concise as possible and that can serve as a tool to communicate NIDCR's identity, priorities, and value to the Institute's diverse constituents. NIDCR anticipates that the update to the plan will be a streamlined and inclusive process that will yield a document which will be practical for the next 5 years and will complement NIDCR's effort to identify scientific opportunities for 2004-09 (see above). NIDCR envisages convening a core planning group and ad hoc meetings to seek broad input. Dr. Frank Macrina will represent the Council in this effort.

Discussion. The Council asked whether the process would include evaluation of the previous strategic plan and linkage with the Institute's evaluation plan. Dr. Garcia commented that evaluation will be an important part of the updated plan, but recognized that a formal evaluation of the current strategic plan may be hampered by its breadth and lack of quantifiable objectives. The Council encouraged NIDCR to highlight the unique "value-added" nature of NIDCR research in both plans. The Council also urged NIDCR to develop an interactive and changeable strategic plan that would last beyond 5 years and to adopt a planning process that can incorporate both a "top-down" and a "bottom-up" approach.

Research Capacity Building in Dental Schools

Dr. Martinez reported on the progress made in developing an RFA for Planning Awards for Research Infrastructure and Capacity Building in Dental Schools. The Council approved the concept for these awards at its previous meeting in January. NIDCR is developing this initiative in response to proposals and discussions at the October 2001 meeting on "Conducting and Putting Science Into Practice: The Critical Role of Dental Schools," which was cosponsored by the Institute and major U.S. dental professional associations.

Dr. Martinez said that the draft RFA is in review and that NIDCR expects to release it in June. Letters of intent would be due in August, applications would be due November 1, and awards would be made by June 1, 2003. The objective of this initiative is to provide resources for U.S. dental schools to develop and implement comprehensive plans to improve their research infrastructure, recruit research personnel, and establish cooperative links. Awards would be made in two phases: the first phase (1 year) would support development of a plan; the second phase (2 years) would support implementation of the plan. Awards for the second phase would be based on the merits of an institution's plan developed during the first phase, the institution's receipt of matching funds, and evidence of the institution's commitment to the effort. Dr. Martinez described the types of activities that could be supported during the planning and implementation phases. An evaluation report will be required at the end of the implementation phase. Dr. Martinez noted that NIDCR anticipates utilizing the cooperative agreement (U) mechanism to fund these awards and, depending on the availability of funds, may reissue the RFA in June 2003, for funding of a second set of awards in June 2004. To prepare for the first set of awards, NIDCR plans to convene regional workshops during August-

September 2002 to inform dental school faculty, students, and research administrators about the RFA; science opportunities; and NIDCR's portfolio, priorities, initiatives, and training programs.

Discussion In response to questions from the Council, Dr. Martinez elaborated on the nature of the planning awards. He commented that NIDCR expects to allocate \$1.5 million for the first planning phase, which could support up to 10 awards at approximately \$150,000 each, and depending on the availability of funds, hopes to award \$1 million per year for 2 years to each institution supported during the implementation phase. Dr. Tabak noted that NIDCR may stagger the awarding of phase-1 grants to enable the Institute to modify later awards based on "lessons learned." If NIDCR staggers the grants, initial awards would be made to nonresearch-intensive schools (i.e., those receiving less than approximately \$6 million in NIDCR support), with subsequent awards made more broadly. NIDCR also will encourage nonresearch-intensive schools to partner with research-intensive institutions when submitting applications.

The Council complimented NIDCR for developing this initiative and for cosponsoring the October 2001 conference. The Council particularly liked NIDCR's plan to stagger awards and to emphasize support for nonresearch-intensive dental schools and linkages between these schools and research-intensive institutions. Members noted that the initiative demonstrates the value of NIDCR and that the measure of success of the program will be the creation of research enterprises in dental schools that are "at the margins." They suggested that NIDCR adopt different approaches for building research capacity among "have" and "have not" schools and give institutions sufficient flexibility to develop appropriate and effective partnerships. The Council also emphasized the need to ensure that institutions make an enduring commitment to research and that the research is innovative and focused on answering scientific questions unique to oral, dental, and craniofacial research.

In addition, members encouraged NIDCR to include site visits in the review of applications and to ensure that awardees meet specific criteria of accountability (e.g., demonstrated interdigitation of research and training, clinical research). Dr. Tabak agreed that site visits will be important and that the research proposed must include a training component. Members expressed some concern about the appropriateness of the cooperative agreement mechanism and about some dental schools' ability to match and leverage NIDCR funds. Dr. Tabak noted that NIH has successfully used this mechanism for many years to support initiatives at academic health centers and that it will enable NIDCR to more closely monitor and follow progress. Dr. Kleinman commented that NIDCR anticipates that the initiative will have a complementary and catalytic effect in stimulating additional funding for research at dental schools. For example, through NIDCR's encouragement, the National Center of Research Resources (NCRR) has begun to receive applications from dental schools for its Centers of Biomedical Research Excellence (COBRE) program, and NIDCR is coordinating with the American Dental Education Association, the American Association for Dental Research, and other organizations to increase dental schools' involvement in research and to elicit other sources of funding. Dr. Tabak added that NCRR's outreach to dental schools has been extremely helpful and collegial.

VI. CONCEPT CLEARANCES

NIDCR staff presented seven concepts for the Council's consideration. As Dr. Tabak noted in his opening remarks, these concepts form the basis for NIDCR's portfolio in translational research for the

coming years. Following staff's presentation of the concepts, the Council engaged in a general discussion.

Translational Research in Dental Practice-Based Tobacco

Dr. Patricia S. Bryant, Health Scientist Administrator and Program Director, Behavioral and Social Science Research Program, Division of Population and Health Promotion Sciences (DPHPS), presented a concept for two proposed RFAs to encourage translational research involving use of dental settings to promote tobacco control (prevention and cessation). The objectives are to (a) characterize critical processes that underlie the translation of science-based findings on oral health impacts of tobacco use into clinical practice behaviors of dental professionals, and (b) develop and test innovative interventions to increase use of effective prevention and cessation procedures in dental education or practice settings. Dr. Bryant said that, despite existing guidelines and knowledge, most U.S. dental clinicians are not fully implementing effective tobacco control approaches. One RFA would target dental education in dental schools, and the second would target general practitioners and dental specialists. Dr. Bryant noted that NIDCR is partnering with the National Institute of Drug Abuse (NIDA) on this 5-year initiative and that NIDA has committed a preponderance of the funding to support awards beginning in FY 2003.

Discussion. The Council noted that the concept was excellent. Members commented on the importance of reimbursing dental practitioners for diagnostic procedures, as an effective way of changing the perceived value of these procedures and their behaviors; the possibility of universities obtaining additional funding from state-level tobacco settlements; and the opportunity to disseminate information through community-based organizations.

The Council unanimously approved the concept.

Temporomandibular Joint Disorders: A Model for Complex Diseases

Dr. Eleni Kousvelari, Chief, Cellular and Molecular Biology, Physiology, and Biotechnology Branch, Division of Basic and Translational Sciences (DBTS), presented a proposed RFA to stimulate multidisciplinary, cross-cutting, and integrative research to delineate the mechanisms underlying the etiology and pathogenesis of orofacial structures associated with temporomandibular joint disorders. The ultimate goal is to encourage a systems approach (from gene to molecule, cell, tissue, and organ) that will enhance understanding of these complex disorders and lead to development of new insights for their treatment and management. Applicants would be encouraged to utilize registries of patients and tissue samples. Research areas would include developmental biology, genetics, and proteomics; bioimaging and bioinformatics in order to delineate the pathophysiology of orofacial muscles; the mechanisms of orofacial pain; and comorbidities. Furthermore, the RFA emphasizes the need for the development and improvement of animal models and for the development of new therapeutics.

Discussion. The Council noted that this concept addresses many important questions and is an excellent example of NIDCR's value-added research that should be publicized. **An expressed concern was that the title may be misleading and that the concept is incomplete because it does not include the "behaving person."** It was noted that the costly risk factors of temporomandibular disorders are more behavioral than biological or pathological; measures of

pain can only be gained by asking persons affected; and psychosocial and gender issues are tremendously important in the seeking of treatment. The concept also does not include pathology in muscles, where the great preponderance of these disorders occur. The Council urged NIDCR to revise the concept to (a) change the title to "Temporomandibular Muscle and Joint Disorders (TMJDs): A Model for the Pathobiology of Complex Diseases," and (b) add the "behaving person" (e.g., psychosocial aspects) to the list of potential research areas. Dr. Kousvelari noted that the concept will include gender differences regarding pain and the measurement of pain and that NIDCR is developing another initiative that will focus on pain and behavioral aspects of temporomandibular disorders.

The Council unanimously approved the concept as amended by the Council.

Longitudinal Prospective Cohort Patient Registry (LPCPR) for TMJDs

Dr. Maria Teresa Canto, Health Scientist Administrator and Program Director, Population Sciences Program, DPHPS, presented a proposed Request for Proposals (RFP) to establish and maintain a national registry to study the natural history of TMJDs. Overall goals for the registry are to establish standardized inclusion and exclusion criteria for potential cases; collect, process, and store patients' information and biological specimens; and serve as a resource for qualified researchers studying these disorders. Dr. Canto indicated that research to understand the etiology of TMJDs is hampered by the lack of population-based epidemiological data and well-designed longitudinal studies. Applicants would have to include the description of a plan to establish an independent oversight committee for the registry.

Discussion. The Council commented that the concept is very good. The Council encouraged NIDCR to include a full range of measures of TMJDs and to ensure that the research and registry in this initiative are linked with the research proposed for the other initiative on TMJDs (see above).

The Council unanimously approved the concept.

Restoring Orofacial Tissues and Organs Using Biomimetic Approaches

Dr. Kousvelari presented a proposed RFA to encourage research on biomimetics and tissue engineering for repair and regeneration of orofacial tissues and organs. The initiative is focused on restoration and regeneration of teeth and periodontal tissues; construction of an artificial salivary gland; strategies for repair and regeneration of temporomandibular structures; and in vivo molecular imaging technologies for determining interactions of implantable materials with biological systems.

Discussion. The Council noted that the initiative is far-reaching and exciting.

The Council unanimously approved the concept.

Innate Mucosal Immune Factors in the Pathogenesis of HIV

Dr. Dennis F. Mangan, Chief, Cellular and Molecular Biology Branch, DBTS, presented a proposed RFA to define the innate factors of the oral mucosal immune system involved in resistance to the

acquisition and spread of HIV and associated opportunistic infections. Recent epidemiological evidence indicates that exogenous infection with HIV, which could occur during receptive oral sex, is extremely rare, in contrast with the relative ease of infection when other mucosal surfaces such as anal and vaginal tissues are exposed to HIV. Dr. Mangan noted that research on innate immunity is a very active field and that investigators are rapidly increasing their understanding of host defense against infectious microbes. With this initiative, NIDCR would encourage research on the full range of innate factors in the oral cavity, which includes salivary mucins, histatins, hypotonicity, cytokines/chemokines, beta-defensins, host inflammatory responses, and antiviral factors produced by epithelial cells and leukocytes. This research would complement existing research supported by NIDCR and potentially lead to development of novel microbicides and targets to enhance resistance to mucosal infection. Dr. Mangan noted that NIDCR continues to be committed to supporting a comprehensive biomedical and behavioral research program to understand the biology of HIV infection, develop effective therapies, and design interventions to prevent new infections.

Discussion. The Council suggested that NIDCR add "oral microbial ecology" to the list of research areas to be studied under this initiative. Elaborating on the evidence to support the initiative, Dr. Mangan said that epidemiological studies indicate a risk of < 1 percent for transmission of HIV infection via the oral cavity, but that data from animal studies show a higher risk of transmission. The research proposed may help to clarify the mechanism(s) and resident factors in the oral cavity that account for this difference.

The Council unanimously approved the concept.

Oral Mucosal Vaccination Against HIV Infection and HIV-Related Opportunistic Infections

Dr. Mangan presented a proposed RFA to support research that would better define ways to exploit the oral cavity to immunize against HIV and AIDS-related opportunistic pathogens. He noted that the oral cavity is potentially an accessible and easy point of entry for vaccines against HIV/AIDS and related infections, but has not been effectively exploited yet. Mucosal immunologists have found that all mucosal tissues appear to be linked to a global mucosal system in which immunization at one site confers protection at other mucosal sites, and recent research suggests that oral and nasopharyngeal vaccines may elicit significant mucosal antibody responses at other mucosal sites. The initiative would focus on identifying ways to deliver effective antigens, developed at the NIH and elsewhere, via the oral route. It would build on existing research supported by NIDCR and NIAID and would capitalize on recent advances in mucosal immunology.

Discussion. The Council supported the concept as a good research area to develop. In response to questions, Dr. Mangan noted that this concept, combined with the previous concept (see above), offers a more comprehensive approach to understanding immunization of the immune system via the oral cavity. If investigators can achieve effective vaccination via the oral route in animal models, they can then compare the efficacy of different approaches (e.g., in oral, anal, vaginal tissues) and alternative ways to boost the immune system. Vaccination via the oral cavity may enhance innate immune factors and stimulate acquired immune function. Most of the research is expected to be done in animal models first, and antigens that are found to be effective will be accelerated into human clinical trials of vaccines. Dr. Mangan also noted that while

industry supports research on systemic vaccination, NIDCR is a leader in research on the much more complex mucosal immunity.

The Council unanimously approved the concept.

Multi-Center Clinical Trials for Management of Dental Caries

Dr. Philip Fox, Consultant, DPHPS, presented a proposed RFA to support multi-center clinical trials of immuno- or chemotherapeutic interventions for management of dental caries. Studies could focus on prevention or treatment of early lesions in children or adults. Dr. Fox suggested that NIDCR would fund one or two phase-3 trials or a larger number of phase-1 or phase-2 studies. Dental caries is the most common chronic infectious disease in the United States and is a notable example of health disparities. While caries rates are declining overall, dental caries is clustered among minority children, older persons, and individuals who are economically underprivileged, chronically ill, or institutionalized. Dr. Fox noted that management of caries as a preventive, nonsurgical intervention is an emerging approach and that expansion of this research area promises to significantly affect disparities in oral health and clinical practice. Immunotherapeutic interventions would likely be in the form of a vaccine or selective bacterial modification. Chemotherapeutic interventions could utilize antimicrobial approaches or other interventions directed at other components of the cariogenic process (e.g., acid-induced demineralization, formation of bacterial biofilm). The objectives would be to eliminate or significantly reduce cariogenic bacteria in the oral cavity and to significantly decrease dental caries. NIDCR anticipates that the studies would be performed in individuals with a high rate or risk of caries. Dr. Fox added that the concept is justifiable because of recent scientific advances, NIDCR's current support of eight clinical trials in childhood or adult caries, the availability of potential agents, and the high program priority for this topic.

Discussion. The Council supported the concept as an excellent initiative that would translate the results of basic science to clinical research.

The Council unanimously approved the concept.

General Discussion

The Council asked whether NIDCR's existing portfolio and resources could accommodate the proposed new initiatives. Dr. Tabak said that the initiatives presented relate to increases proposed in the President's Budget for FY 2003 and that support for each initiative, and the priorities within and among initiatives, will depend on criteria of program relevance and on available funds. Dr. Tabak also noted that the ongoing evaluation of NIDCR's portfolio is likely to redirect some of the Institute's resources to the new emphasis on translational and clinical research. He suggested that the time is ripe for NIDCR to move forward with translational and clinical research and that the Congress will support effective interventions and increased basic science to underpin these interventions. By funding strategic clinical trials, NIDCR hopes to improve the practice of dentistry in the United States.

The Council expressed strong support for some redirection of NIDCR's portfolio and noted that all the concepts presented are very important and exciting initiatives for dentistry. The Council urged

NIDCR to communicate its new emphasis as an overarching theme in the revised strategic plan and more broadly to NIDCR's constituents and external audiences. Dr. Tabak noted that the concepts will be posted on NIDCR's Web site and that staff would communicate the Institute's interests during visits to dental schools. He encouraged the Council members to share information about these initiatives throughout their institutions and among their colleagues. In response to Council's specific suggestion that his remarks be transcribed and forwarded to all dental schools, Dr. Tabak noted that NIDCR is preparing a communication, which Council will preview, to update all NIDCR grantees and constituents about NIDCR activities and that he may prepare an article for journal publication.

VII. INFORMATION ITEMS

Staff also presented several information items.

Clinical Trials-Related Information Items

Dr. Kleinman described several items developed by DPHPS staff in response to discussions and input from the Council at its two previous meetings, in September 2001 and January 2002. The aim of these efforts is to define and utilize a clinical trials pathway for investigators and staff that would facilitate management of clinical trials, collaboration in areas of research emphasis and priorities, and movement from the planning phase to phase-3 clinical trials. Dr. Kleinman reported that staff conceptualized the concept for this pathway, developed a Clinical Trials Policy Announcement to advertise the concept, and revised two Program Announcements—a Revised Clinical Trial Planning Grant Program Announcement and a Revised Clinical Trial Pilot Grant Program Announcement. All of these materials will be provided on NIDCR's Web site.

In the proposed clinical trials pathway, investigators interested in submitting an application for support of a clinical trial would first submit a brief concept (2-3 pages) for Institute clearance. If the investigator's subsequent application were successful, the Institute would award an initial planning grant (for 1 year and \$100,000) and then a phase-3 study. Alternatively, and depending on the stage of research, investigators may omit the planning stage. Dr. Kleinman noted that inclusion of a concept clearance stage was proposed at the Council's January meeting. It also is a "best practice" used by other institutes and centers (ICs).

Dr. Kleinman described in detail the proposed policy and program announcements. She noted that the two program announcements will be modifications of existing announcements that were issued in August 1999. To fund the grant awards, NIDCR is considering use of the cooperative agreement mechanism. Dr. Kleinman noted that, regardless of the mechanism used, staff will work closely with investigators at all stages to foster effective trials. An important goal is to assure that endpoints and procedures are comparable among clinical trials conducted on the same theme by different investigative groups.

Discussion. The Council noted that the conceptualization of the clinical trials pathway is helpful and that NIDCR's effort is very pro-active and constructive. The Council also commented that the process will demand significant work by staff. Dr. Fox noted that a support contract, which the Council conceptually approved at its January meeting, will help staff perform the management function. The

Council agreed that cooperative agreements are an effective mechanism for supporting clinical trials research. The Council encouraged NIDCR to carefully define and elaborate the parameters of this mechanism, if it is used, because the oral health research community has less experience with it than do other NIH constituents. The Council also encouraged the Institute to look at the Department of Veterans Affairs' cooperative agreement program and infrastructure, for guidance as NIDCR expands its own clinical research effort.

Oral Health Research Curriculum Grants

Dr. James A. Lipton, Acting Deputy Director, DPHPS, and Director, Research Training and Career Development Program, DPHPS, described a proposed program announcement to announce NIDCR Oral Health Research Curriculum (OHRC) grants. The purpose is to infuse an appreciation of science and the results of scientific research in the curriculum of dental schools. Competency in genetics would be a mandatory component. Through these grants, dental scientists and Ph.D. researchers would actively participate in dental students' education, interacting with them through all 4 years of dental school and during postgraduate specialty training. NIDCR would use the NIH Education Research Program grant (R25) mechanism of support. Awards would include planning, implementation, and evaluation phases, and continuing support would be **dependent on achieving the goals of the project**. Grants could be renewed one time only. Initial support would be limited to 4 years, during which a planning phase would be completed by the end of the first year. The remaining 3 (or fewer) years would be used for implementing and evaluating the plan. Funds requested for this program would be limited to \$150,000 per year in direct costs. Dr. Lipton noted that the grants would complement the Planning Awards for Research Infrastructure and Capacity Building in Dental Schools previously described by Dr. Martinez (see section V above).

Discussion. The Council strongly supported this initiative and noted the importance of partnerships between "have" and "have not" institutions to fulfill the objectives of this initiative. In addition, Dr. Lipton referred the Council to a booklet, entitled "Future Oral Health Scientists Present Their Research," which is a compilation of abstracts from posters that NIDCR-supported trainees presented at the 2002 annual meeting of the International Association for Dental Research (IADR). He noted that NIDCR hopes to communicate the research of new faculty more visibly in the future. Dr. John Clarkson, President, IADR, welcomed the opportunity to give this activity more visibility and a higher profile at future IADR meetings.

Interventional Trials in Oral Infectious Diseases

Dr. Fox described a program announcement to express NIDCR's interest in supporting interventional trials that address oral infectious diseases. The goals are to highlight NIDCR interest in this area and to encourage investigators to submit applications for interventional trials, particularly early-stage phase-1 and phase-2 studies, in NIDCR's newly defined clinical trials pathway. Dr. Fox noted that NIDCR would emphasize that all clinical trials, except some phase-1 trials, should be multi-center. He also noted that the selection of the oral infectious diseases area is based on the Council's guidance at its previous meeting in January. Dr. Fox remarked that oral infectious diseases are a critical component of NIDCR's mission, interventional trials in this area are unlikely to be supported by other ICs, and numerous target agents are available for this research. The broad theme of oral infectious diseases would include any oral condition with an infectious cause (bacterial, viral, and fungal), and

NIDCR would give special emphasis to trials in the areas of dental caries and periodontal diseases. The hope is to enhance the translation of current basic science findings into clinical studies.

CLOSED PORTION OF THE MEETING

This portion of the meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

There was a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions, or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect.

VIII. REVIEW OF APPLICATIONS

Grant Review

The Council considered 368 applications requesting \$84,404,029 in total costs. The Council recommended 294 applications for a total cost of \$69,531,597 (see Attachment II).

ADJOURNMENT

The meeting was adjourned at 4:00 p.m. on June 10, 2002.

CERTIFICATION

I hereby certify that the foregoing minutes are accurate and complete.

Dr. Lawrence A. Tabak
Chairperson
National Advisory Dental and
Craniofacial Research Council

Dr. J. Ricardo Martinez
Executive Secretary
National Advisory Dental and
and Craniofacial Research Council

ATTACHMENTS

- I. Roster of Council Members
- II. Table of Council Actions
- III. Director's Report to the NADCRC, June 2002

NOTE: A complete set of open-portion handouts is available from the Executive Secretary.